REMARKS

Claims 245-248, 251, 253, 261-265, 306-307 are pending in the above-referenced application. Claim 251 has been amended to cancel non-elected subject matter. As will be discussed in further detail below, claims 245, 247 and 306 have been amended to more distinctly claim that which Applicants regard as their invention. Claims 247 and 306 have also been amended to cancel non-elected subject matter. Amended claim 245 is supported by the specification on pages 38, lines 8-11, 16-21; page 39, lines 1-3 and lines 7-12; page 41, lines 16-20; page 42, lines 1-2; Examples 5 and 6 and Figures 4 and 6. Amended claims 247 and 306 are supported by the specification on page 40, lines 4-7; page 50, page 52, lines 1-16; Examples 12-15, Figures 4, 15-18.

I. SUBSTANCE OF INTERVIEW

First, Applicants would like to thank Examiner J. Zara for her time and thoughtful suggestions during the interview with Applicants representative, Cheryl H. Agris on May 14, 2010. The Substance of the Interview is set forth below.

A. Brief Description of any Exhibit Shown or any Demonstration Conducted

Applicants submitted annotated page 38-42 and 51 and Figures 4, 6, 15-18 of the specification since these pages and figures were referred to during the interview. Applicants further submitted Figure 1 of Curiel and Columns 2 and 3 (annotated) of Priest.

B. Identification of Claims Discussed

Claims 245, 247, 306 and proposed claim 308 were discussed.

C. Identification of Specific Prior Art Discussed

As will be set forth in further detail below, the cited references, Curiel et al., Priest et al. and Elliot et al. were discussed with respect to the rejections under 35 USC §103.

D. Identification of Principal Proposed Amendments of a Substantive Nature Discussed

Possible amendments to claims 245, 247 and 306 were discussed.

E. Identification of General Thrust of Principal Arguments Presented to the Examiner

An adequate description has been provided to support the pending claims. No new matter is contained in the pending claims. Further, none of the pending claims are obvious over the cited references.

F. A General Indication of Any other Pertinent Matters Discussed

Further possible amendments to claims 245, 247, and 306 were discussed.

G. General Results or Outcome of the Interview

Applicants will set forth arguments as to why the claims are not obvious over the cited references and will point out where there is support for the amended claims.

I. The Obviousness Type Double Patenting Rejections

Claims 245-248, 251, 253, 261-265, 306 and 307 have also been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 275, 289, 290, 296-301 of copending Application No. 08/978,634. Applicants will address this rejection once there is indication of allowable subject matter of the instant application.

Claims 245-248, 251, 253, 261-265, 306 and 307 have also been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 2 of copending Application

No. 11/929,897. Applicants will address this rejection once there is indication of allowable subject matter of the instant application.

II. The Rejections Under 35 USC §103

Claims 245-248, 251, 253, 261-265, 306 and 307 are rejected under 35 U.S.C. 103(a) as being unpatentable over Priest (USPN 5,391,723) (hereinafter "Priest") and Curiel et al. (U.S. Patent 5,521,291) (hereinafter "Curiel et al."), the combination in view of Elliott et al (USPN 5,837,489). The Office Action states with respect to Priest and Curiel et al.:

> Priest (USPN 5,391,723) teaches nucleic acid constructs for target cell delivery comprising a nucleic acid domain linked covalently to a targeting protein domain which is optionally an antibody which is targeted to a target cell epitope, which antibody is optionally monoclonal or polyclonal, and which nucleic acid is linked either directly to the antibody or via a linker, and which nucleic acid conjugates are optionally single or double stranded (see the abstract, col. 2, 6-9, 17-18).
>
> Curiel et al. (U.S. Patent 5,521,291) teach methods, compositions, target cells for delivering compositions to cells in vitro and in vivo, and kits for target cell delivery, which compositions comprise a construct having at least one terminus comprising a polynucleotide tail hybridized to a complementary polynucleotide and an antibody bound to the hybridized polynucleotide (e.g. ribozymes attached to antibodies, or viral nucleic acids for target cell delivery in combination with antisense for target gene inhibition, target cell ligands), and which nucleic acid compositions optionally comprise a domain to a specific nucleic acid component and a domain to a cell of interest, and a different, specific nucleic acid desired to be delivered to said cell, and optionally comprising a binder which is a polymer, or one which mediates ligand binding to a receptor, including lectins, antigens and other receptors (see esp. the abstract; Fig. 1; col. 3-11; 13; 16; example 6, col. 24-29; claims 3, 5, 6, 14 and 15).

The Office Action does concede that :

> The primary references do not teach a nucleic acid domain which is complementary to a linear nucleic acid, and which domain directs synthesis of a nucleic acid product.

However, the Office Action asserts that Elliot et al.

> …teach the design, transfection into target cells and expression of nucleic acid constructs which optionally comprise expression vectors, which are optionally closed plasmids or linear constructs, and which direct synthesis of nucleic acid products….

It is thus concluded in the Office Action that:

> It would have been obvious to design and use a non-natural construct comprising a nucleic acid linked to a targeting protein, and optionally via a linker which also comprises a polymer, and which nucleic acid is complementary to a second nucleic acid, because Priest and Curiel taught nucleic acid constructs comprising self-complementary polynucleotides wherein one of the nucleic acid strands is optionally covalently linked to a targeting protein which is optionally an antibody directed to a target cell epitope for target cell delivery, and is optionally linked via a linker or polymer. One would have been motivated to design and use this composition for enhancing target cell delivery of a nucleic acid construct, relying on the bound targeting protein. It would have been obvious to replace one of complementary (oligonucleotide) nucleic acid strands taught by Priest or Curiel with a longer nucleic acid which directs the synthesis of a nucleic acid product because this allows for the targeting of an expression construct to a desired target cell, whereby a nucleic acid product is expressed rather than solely utilizing the target constructs for delivery of target gene inhibition constructs. To replace one of the strands of a double stranded oligonucleotide delivery construct with a longer nucleic acid strand that directs synthesis of a nucleic acid product would have been a matter of design choice and would have required routine experimentation taught previously in the art, as evidenced by the teachings of Priest and Curiel.
>
> One would have been motivated to have one of the nucleic acid strands as an expression unit that allows for the synthesis of a nucleic acid product because

> this approach logically allows for multiple or alternative uses of a targeting nucleic acid construct, including but not limited to the expression of a recombinant (e.g. therapeutic) gene product within or in the vicinity of a desired target cell, and also allows for the expression of either inhibitory nucleic acids or recombinant proteins at the site of the target cell, increasing their concentration at the target cell site. One of skill in the art would have reasonably expected that the targeting constructs previously taught by Priest and Curiel would provide for enhanced target cell localization of the nucleic acids, thereby increasing the concentration of nucleic acids at the target cell site, in turn allowing for the expression of a desired nucleic acid product in or near the target cell, and allowing for enhanced delivery of therapeutic molecules at a desired target cell site in the body.

Applicants respectfully traverse the rejection. Before addressing the rejection, Applicants wish to point out that that there are three independent claims in the instant application, claim 245, 247 and 306. Applicants further note (a) and (b) of claims 247 and 306 are the same. Thus, Applicants will address the rejection with respect to 245 and dependent claims and claims 247, 306 and dependent claims.

A. The Rejection of Claims 245-246 and 307

Applicants assert that claim 245 as amended would not be obvious over the cited references. Although the two primary cited references, Curiel et al. and Priest describes attachment of an antibody nucleotide, there is no suggestion that a third strand has any particular utility in this arrangement . In contrast, the advantages of such an arrangement are described in the specification where the strand that is used for entry (i.e attached to an antibody) into a cell and also "without substantially interfering with the biological properties of said nucleic acid" (page 34). Specifically, in the Examples depicted in Figures 4 and 6, the cell binding portion, is dispensable after the nucleic acid construct is transported into a cell and can be eliminated from the construct by extension of the linear strand (referred to as the second strand in amended claim 245). Further, page 35 of the specification states, "In cases where ligands or chemical modifications can

interfere with biological activity, chemically modified segments of the CHENAC could be segregated from the construct subsequent to introduction to the cell by displacement or loss of modified segments and page 46 states "Thus, the construct may contain at least one terminus, such a terminus comprising, for example a polynucleotide tail. Such a modified nucleic acid, subsequently introduced into a cell, could be displaced and/or replaced."

Further, Priest describes the use of a modified nucleic acid attached to an antibody where the nucleotide can comprise a singe-stranded or double-stranded polynucleotide without any reference to a third oligonucleotide. No particular problem with the presence of such a modification or consequently no need of a cure for it is described in this reference. Curiel et al. describes an antibody covalently attached to polylysine and this complex being non-covalently bound to a double-stranded nucleic acid. The only particular element that seems to have been introduced by Elliot et al. reference is that linear nucleic acids have been used for transfection. As such the combination of these three references do not result in the composition of amended claim 245.

Claims 246 and 307 depend from claim 245. Thus arguments made with respect to claims 245 would apply to claims 246 and 307 as well.

2. The Rejection of Claims 247, 248, 251, 253, 261-265 and 306

Applicants assert that amended claims 247 and 306 provide a clear recitation of the compositions set forth in Figures 4, 15, 16, 17 and 18. It is Applicants' further belief that the particular arrangements of nucleic acids that are described by the current claim language is not made obvious by the cited art. In the present invention, a nucleic acid is used as a linker to join a nucleic acid construct to a cell specific binding agent.

In Curiel et al., polylysine is used as the linking agent. No polynucleotide in Curiel is used to link an expression vector to a cell specific moiety.

Priest only teaches the covalent attachment of a moiety of interest to a polynucleotide that may be either single or double-stranded, the use of a polynucleotide as a linker separate from the polynucleotide of interest is not taught. As such, there is direct attachment of an antibody to a double-stranded

nucleic acid in Example 4 of Priest for creation of a complex that can be used to convey intercalators into a cell. There is certainly no mention of two double-stranded regions.

Clearly, there is no particular need or use described for the presence of two double-stranded regions in Curiel or Priest whereas in the present invention, hybridization to a linker is part of one double-stranded region and functionality of the vector is endowed by the presence of a second double-stranded region. In Figure 5 of the disclosure, the second double-stranded region can provide a means for separating the linker polynucleotide from the vector after introduction into the cell and Figure 15, Figure 16, Figure 17 and Figure 18 describe the presence of double-stranded self-complementary ITR's at each end that are required for replication of AAV.

Applicants would further like to point out that Priest and Curiel et al. do not teach or describe "self-complementary polynucleotides" since this term is understood in the art to refer to intrastrand complementary base pairing (within single strand) whereas and Priest and Curiel describe interstrand hybridization between two separate strands of DNA and as such they teach "complementary polynucleotides".

As noted above, Elliot et al. merely discloses that linear strands can be transfected. Otherwise, this reference is of no significant relevance with respect to the instant claims.

Thus, even if the all of the references were combined, one of ordinary skill in the art would not obtain the composition or kit of the present invention. Thus, claims 247 and 306 would not be obvious in view of the cited references.

Claims 248, 251, 253, 261-265 depend from claim 247. Thus arguments made with respect to claim 247 apply to these claims as well.

In view of the above arguments and amendment of claims 245, 247 and 306, Applicants assert that the rejection of claims 245-248, 251, 253, 261-265, 306 and 307 under 35 USC 103 have been overcome. Thus, Applicants respectfully request that the rejection be withdrawn.

IV. Conclusion

It is Applicants belief that the pending claims are in condition for allowance. However, if a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney request that he be contacted at the number provided below.

Respectfully submitted,

/Cheryl H Agris/

Dated: May 22, 2010

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